

What is claimed is:

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1. A method for screening neural system defects in a mammal, said method comprising:
 - (A) providing chromosomal material from said human;
 - (B) detecting a modification of the *NAP1L2* gene in the chromosomal material, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, d) insertion aberent or e) altered epigenetic control; that causes a loss of biological function in the *NAP1L2* gene; and
 - (C) correlating the modification of said gene with a potential for a neural system defect.
2. A method according to claim 1 where the said screening of neural system defects concerns a human being.
3. The method of claim 1, wherein said modification in the *NAP1L2* gene is detected by hybridization with a labeled probe.
4. The method of claim 3 wherein said probe is a oligo-nucleotide probe of SEQ ID NO:3.

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5. A method of claim 1, wherein said modification is detected by
 - (A) amplification of the chromosomal material using PCR;
 - (B) sequencing said material to detect the modification of the nucleotide sequence; and
 - (C) correlating the modification of said gene with a potential for neural system defects.
6. A method for screening neural system defects in a human, said method comprising:
 - (A) providing biological material from said human;
 - (B) detecting the absence, inappropriate, or modified expression of *NAP1L2* gene product using labeled antibodies to said gene product; and
 - (C) correlating said absence, inappropriate, or modified expression with a potential for neural system defects.
7. The method of claim 5, wherein the said antibodies are polyclonal.
8. The method of claim 5, wherein the said antibodies are monoclonal.

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9. A method of any one of claims 1 to 8, wherein the neural system defect results from a failure of or incomplete neural tube closure.

10. A method of claim 9, wherein said incomplete neural tube closure results in spina bifida.

11. The method of any one of claims 1 to 8, wherein the neural system defect results from inappropriate control of nucleosome activity in neurons.

12. The method of any one of claims 1 to 8, wherein the neural system defect results from inappropriate control of the cell cycle in neurons.

13. The method of any one of claims 1 to 7, wherein the neural system defect results from inappropriate differentiation of neurons.

14. The method of any one of claims 1 to 7, wherein the neural system defect results from inappropriate maintenance of neurons.

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15. A recombinant polynucleotide comprising a nucleotide sequence, wherein said sequence includes at least one

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modification of the *NAP1L2* gene, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, d) insertion, or e) site-directed mutagenesis that causes a loss of biological function in the *NAP1L2* gene.

16. A recombinant polynucleotide comprising a nucleotide sequence including at least the *NAP1L2* gene and its promoter included in SEQ ID NO:4.

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17. The polynucleotide of claim 15 or 16, wherein said polynucleotide is a chromosome or a part of it of a neural cell.

18. A neural cell containing the polynucleotide of claim 17.

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19. The neural cell of claim 18, wherein the cell is derived from an immortal cell line, such as embryonic stem cells, neuronal cell line, or tumor derived cell line.
20. The neural cell of claim 18, wherein the *NAP1L2* gene is under control of a neural-specific promoter, such as nestin, other neuronal members, and inducible promoters.

21. The neural cell of claim 17 or 19, wherein the neural cell is from a wild-type animal.

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22. The neural cell of claim 18, 20, or 21, wherein the *NAP1L2* gene is modified, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, d) insertion, or e) site-directed mutagenesis that causes a loss of biological function in the *NAP1L2* gene.

23. The neural cell of claim 18, 20, or 21, wherein the *NAP1L2* gene is altered through a naturally occurring mutation.

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24. A polynucleotide comprising the promoter of the *NAP1L2* gene in SEQ ID NO:4, or a polynucleotide hybridizing under stringent conditions with SEQ ID NO:4, or at least 20 nucleotides of said SEQ ID NO: 4.

25. A vector containing the polynucleotide of claim 24.

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26. A method of making a recombinant neural cell comprising:
(A) providing a neural cell;
(B) modifying a *NAP1L2* gene or the promoter of the *NAP1L2* gene in the neural cell, wherein said modification is selected from a) substitution,

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b) deletion, c) frame-shift, and d) insertion that causes a loss of biological function in the gene; and

(C) selecting modified cells.

27. A method of screening for therapeutic compounds comprising:

- (A) providing a cell of any one of claims 18 to 23;
- (B) introducing to the cell a compound to be screened; and
- (C) correlating change in the proliferation of cells with the activity of the compound.

28. A method of screening for therapeutic compounds comprising:

- (A) providing a transgenic knockout animal containing the human *NAP1L2* gene in its chromosomes.
- (B) introducing to the animal a compound to be screened; and
- (C) correlating a change in the development and maturation of the nervous system with the activity of the compound.

29. A method for screening neural system defects in a mouse, said method comprising:

- (A) providing chromosomal material from said mouse;

- (B) detecting a modification of the *Nap112* gene in the chromosomal material, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, or d) insertion that causes a loss of biological function in the *Nap112* gene;
- (C) correlating the modification of said gene with a potential for a neural system defect.

30. A method for screening neural system defects in a mouse, said method comprising:

- (A) providing biological material from said mouse;
- (B) detecting the absence, inappropriate, or modified expression of *Nap112* gene product using labeled antibodies to said gene product; and
- (C) correlating said absence or inappropriate expression with a potential for neural system defects.

31. A recombinant polynucleotide comprising a nucleotide sequence, wherein said sequence includes at least one modification of the *Nap112* gene, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, d) insertion, or e) site-directed mutagenesis that causes a loss of biological function in the *Nap112* gene.

32. A polynucleotide comprising the promoter of the *Nap112* gene in SEQ ID NO:1, or a polynucleotide hybridizing under stringent conditions with SEQ ID NO: 1, or at least 20 nucleotides of said SEQ ID NO: 1.

Sub All 33. A vector containing the nucleic acid molecule of claim 32.

34. A recombinant neural cell comprising a vector comprising the *Nap112* gene.

35. The neural cell of claim 34, wherein the *Nap112* gene is under control of a neural-specific promoter, such as nestin or other neuronal genes or inducible promoters.

36. A recombinant neural cell of claim 35, wherein the *Nap112* gene of the native cell is modified, wherein said modification is selected from a) substitution, b) deletion, c) frame-shift, d) insertion, or e) site-directed mutagenesis that causes a loss of biological function in the *Nap112* gene.

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37. A method of screening for therapeutic compounds comprising:
- (A) providing a cell containing a polynucleotide according to claim 32;
 - (B) introducing to the cell a compound to be screened; and
 - (C) correlating change in the proliferation of the cell with the activity of the compound.

38. The method of claim 37, wherein said change in proliferating cells is a control of cancer of neural cells.

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39. Use of therapeutic compounds obtained by the method according to claim 27 for increasing the expression of *NAP1L2* gene in tumoral human neural cells or for decreasing the expression of *NAP1L2* gene in human neural cells afflicted by a degenerating disease.

40. An eukaryotic cell containing the insert comprised in the plasmid pBPX1 or pBPX2 or pBPX3 or polynucleotide hybridizing under stringent conditions with the said insert.

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41. A plasmid consisting in the deposit made at C.N.C.M.
under the Accession Number I-2463.

42. A plasmid consisting in the deposit made at C.N.C.M.
under the Accession Number I-2464.

43. A plasmid consisting in the deposit made at C.N.C.M.
under the Accession Number I-2465.

44. A plasmid consisting in the deposit made at C.N.C.M.
under the Accession Number I-2466.

45. A polynucleotide containing the sequence SEQ ID NO:6

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Genomic sequence BPX human

1. acctaaaggaaaaatttatctataaactgacagaatttagaaaataacacacaatatgtaaacaggttttaatatctgtg
2. atagtaacaaattcttttaaatctggaaaaataatagtcaatttaaaattttcaatttaataatgatccaaag
3. ttagaataatgaacaaaataaactcccaataattactatagagaggaaatttaattactgcaaagcttcccatctta
4. caaatacattatcaaatagtttaaccatttctttaatgctgagatttagattatttcccaattaaactcaaaagcatcaagc
5. aaatgttatgatttctaaagataaacataactttccatttttggttttgtatatagtatatttcaacggctgttaaaag
6. ccagcattaaaggaggaagcagaaagttagtattgggactgggtgtatttataagccagggaactgggttaattgtgggt
7. aattgtctgggtatgtttactagtcaagtagctgtatatacaccatactagtttttcatcacaggccctcattcgccccact
8. gccatcggacttctctctctctccctcacaggaaatgtttcgagaatttttcaacctaaaatcatatagcttgtgaaaaa
9. taccgacaaaacataatatagaataatttaataaactgcacgccaccctaaagaccatcagtgctaatctctgggtgtttta
10. atcttttgagcgtttgtttatcagctcttccaccatccacctctccctccccagggtccccgatctaaaatcaagagat
11. cgatttaggatgggtgggtgctttgtctctctcattgttcgacatttagttacgtttctctgagctctctggaaagc
12. ataaaagtataataatctgtttaaagttggatgaatcagccatgttagagagcctgggaaggtgagcagagttgaaacttgatag
13. ggctagaggacgaggaggaggtggatgaatcagccatgttagagagcctgggaaggtgagcagagttgaaacttgatag
14. atctaataatttactggctctgggtttgtcagtcactacattgcagcaaatgagattagagatagttgtgggagggag
15. gagggtgacgcagcaatctatttgcacctagaaaattttaggcaagtgtatagctgcgtaacatcactgcggcaccgttttt
16. tcttgcagcagtagctgtctgtcggaggaggtctgccactgcagctctctgcagctctccggctctctctgcaggaatcgg
17. tcaacgcagcgtctgcggccctctgcacccagccaggtgccactgcttcagtcgggttctcaaaagctcagcaccatc
18. ttttatccccgagcagctggatcgtcgtttctcagtcgggacgccactgctaggtccgaccccgctctctgatat
19. ttcgggtgagctctttctctgtggaggtttgggtctcccgatctctctgtgtagccacttaggggtgtacggtctcttgaaaa
20. atggccgagtcagagAACCGCAAGGAGCTGTCAGAAATCCAGTCAAGAAGAGGGCTGGTAATCAGATAATGGTGGAGGGCT
21. CGGGGAACATCTGGAGCGCGGTGAAGAAACGGTGAAGATACTGCTGCTGGGTCCGGGAAGATGGGAAAAAGGTGGCGATCTGAT
22. GGCTTGGGGAAGAAGGGGAAAAACGGTGAAGATACTGCTGCTGGGTCCGGGAAGATGGGAAAAAGGTGGCGATCTGAT
23. GAGGACTCAGAGGCGACGCTGCCAAAGGACTTATCGGTTATGTTTAGATACAGACTTTGTTGAAAGTCTACCTGTGAA
24. AGTTAAGTACCCTGTGTTTGAAGCTTCAACCTTAAAGCTTAGAGCGGCCAATTTAGAAATCCAAATTCCTGAGGGAATTTT
25. ATGACATTGAAGAAAAGTTTGCTGAATGTACCAACCCTTACTGGAAAAAGAGCGTCAGATCATCAATGCAATCTATGAA
26. CCTACAGAAGAGGAATGTGAATATAATCAGACTCTGAGGACTCTGATGATGAGGAAATGTGTCATGAAGAGATGTATGG
27. TAATGAGGAGGGTATGGTACATGAATATCTGGATGAGGACGATGGTTATGAGGACTATTATTATGATTATGCTGTGGAAG
28. AGGAGGAGGAGGAGGAGGAGGAGGAGGACGACATTGAGGCTACTGGAGAAGAGAAATAAGAGAGGAGGATCCTAAGGGAAT
29. CCGTATTTTGGCTAACTGTTTAAAGCTTTCAGATCCTCTGATTAAGAAATATGATGAGCCTATTCTGAA
30. GCTCTGACAGATATTAAAGTTAAGCTTTCAGATCCTGGCGAGCCCTCAGTTTCAACACTAGAATTTCACTTCAACCCCA
31. ATGAATATTTCAAAATGAGTTTGTGACAAAGACCTATGTGCTGAAGTCAAAGCTAGCATATTATGATCCCATCCCTAT
32. AGGGGAACCTGCCATTGAGTATTTCCACAGGCTGTGAGATAGATTGGAATGAAGGAAGAATGTCATTGAAAAACCATCAA
33. GAAGAACACAGAACATCGGATCTGGGGAACAATCCGAACCTGTAACCTGAAGATTTTCCCAAGGATTCATTTTCAATTTT
34. TCTCTCTCATGGAATCACCTCAAATGGAAGGGATGGAATGATGATTTTACTTGGTCACAATTTACGTACTTACATA
35. ATTCCAAGATCAGTATTATTTTCTCAGGTGATGCATGGAATCTCAGCAGGAGGGGGTAGGTAGAGAAGTTAATGATGC
36. AATTTATGACAAAAATTTATTTATGATAATTTGGATGGCTGCAATTGAGGAAGTTAAAGCTTGTGCAAAAAACCTTGAGGCAT
37. TAGTAGAAGACATTGATCGTTAGAGCagagtatacaggccctgaaatttaactgccctagatatagttactcaaggtata
38. agaagccttgtgtctgtattttgctttgtagtgttagttaaacaatagtttcaaaaaataaagaaaagttcaaaaact
39. aatttaatttgaccttgagtttttagtagtagaattgtttcaagaaatgtacactgtggttaaagatttaaacactagtat
40. agtgttgtgtagctttaaactcttctgaagtcttttctgcatgtagctttaactctgtggtatgaaatgatcagaaatgct
41. aagttagaccaatatttgtttggaaaaaaaactctgggaaacaacccaaggggtttctgctgttgtgttttcttttct
42. atttttgttttacttagtcttttagctagtggatttaattttgttgcctgcttcatatttgcataaacaatgagcagtagaa
43. ttttaaaacttggtgcttaagaggcctgcataagataagaatttcaggcaaaactacatttattgtttaataacagcttg
44. ttcataaggctcttctgtattttatgttaactgtgataaataatgaaaacttagttataattgaggtattgttctgtcggtaga
45. tgttagtcagatttttcaaaagtgtgcacataattgtctgtgtaattgtgtaagccataattacaggtttaattctc
46. ttttctattacatcatttcattgaaagctgacactttaccattttgaaaagatatttctgttctttctcagtgtaaaaaa
47. aaagaataaaaaatttcaga

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46. The polynucleotide of claim 24, wherein said polynucleotide further comprises an heterologous amino acid sequence coding for an heterologous polypeptide under the control of *NAP1L2* promoter.
47. A vector containing the polynucleotide of claim 46.
48. A neural cell containing the polynucleotide of claim 46.
49. A process for targeted expression of a polypeptide in a neural cell wherein said neural cell is a cell according to claim 48.
50. The polynucleotide of claim 32, wherein said polynucleotide further comprises an heterologous amino acid sequence coding for an heterologous polypeptide under the control of *Nap1l2* promoter
51. A vector containing the polynucleotide of claim 50.
52. A neural cell containing the polynucleotide of claim 50.
53. A process for the targeted expression of a polypeptide in a neural cell wherein said neural cell is a cell according to claim 52.

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